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Remarks

Claims 1-7 and 10-14 were pending in the subject application. By this Amendment, claims 1, 2, 4, 5, and 10-12 have been amended, and claims 7 and 14 have been cancelled. The undersigned avers that no new matter is introduced by this amendment. Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 1-6 and 10-13 are currently before the Examiner for consideration, and favorable consideration of the claims is respectfully requested.

By this Amendment, the applicant has amended the claims to correct obvious typographical errors and to recite that a plurality of hematopoietic stem cells are administered. Support for this amendment can be found, for example, at page 5, lines 19-23, and throughout the specification as filed.

The specification has been objected to on the grounds that the specification lacks a detailed disclosure regarding stem cell transplantation. The Office Action indicates that the abstract referred to at page 6 of the subject specification does not contain detailed information regarding stem cell transplantation. The undersigned gratefully acknowledges the courtesy extended by Examiner Qian during the telephonic conference conducted on December 1, 2003. As discussed during the telephonic conference, the "Abstract" mentioned at page 6, line 21, of the specification refers to the Chopp *et al.* abstract (the citation of which is provided in the preceding paragraph at lines 16-20 of the specification), as opposed to the abstract of the specification (which was submitted with the applicant's preliminary amendment). The Chopp *et al.* abstract describes intracerebral transplantation of hematopoietic stem cells in mice. Further guidance regarding the intracerebral transplantation procedure is provided throughout the specification. Accordingly, reconsideration and withdrawal of the objection is respectfully requested.

Claims 1-7 and 10-14 have been rejected under 35 U.S.C. §112, first paragraph, as non-enabled. The applicant respectfully submits that the claimed invention is fully enabled by the subject specification.

The Office Action indicates that, at the time of filing the subject application, the state of the art was such that it required undue experimentation to make and use the claimed invention. At page

4, the Office Action states that the specification does not provide any details regarding what type of hematopoietic stem cells were transplanted into the mice. Donor cells were harvested from mice, as indicated at lines 10-11 of the Chopp *et al.* abstract. However, as taught at page 4, lines 22-24, human cells are preferably used in the treatment of human patients.

At pages 4 and 5, the Office Action states that it is unclear whether hematopoietic stem cells have the potential to develop into neurons, glia, and astrocytes upon intracerebral transplantation. As indicated at lines 14-20 of the Chopp *et al.* abstract, the phenotypic fate of donor cells was determined using immunohistochemistry, which showed that scattered bone marrow cells, hematopoietic stem cells, and mesenchymal stem cells expressed the neuronal or astrocytic phenotype. Furthermore, the Office Action indicates that it is unclear whether human cells have the same potential as mouse cells. As the Examiner is aware, the teaching within the specification concerning the manner of making and using the subject invention must be taken as true unless the Patent Office can cite specific reasons to doubt the objective truth of the statements contained therein. *In re Marzocchi* 169 USPQ 367 (CCPA 1971). The Office Action cites page ES-6 of the NIH publication ("Stem Cells: Scientific Progress and Future Research Developments") for its observation that human cells and mouse cells differ in various ways. Although the NIH publication indicates that laboratory conditions favoring growth and specialization of cells may differ among human and mouse cells, the NIH publication does not indicate that the cells exhibit wholly different differentiation patterns *in vivo*. Furthermore, the Mezey *et al.* publication merely indicates that those studies have yet to be carried out (page 301). Thus, based on the cited references, there is no rationale for presuming that while mouse hematopoietic stem cells differentiate into neural cells *in vivo*, human hematopoietic stem cells do not exhibit a similar plasticity. Furthermore, the methods of the subject invention require administration of hematopoietic stem cells into the patient, wherein they differentiate *in vivo*. It is therefore unnecessary to obtain distinct cell types prior to administration. Moreover, submitted herewith is the Weimann *et al.* publication, which shows that human bone marrow cells do indeed have the capability of forming effective neural cells in human adult brains.

The Office Action cites the NIH publication as showing that there are difficulties in cell-based transplantation therapies. However, the NIH publication does not indicate that stem cell

transplantation will not work. With any type of therapy there are always likely to be issues that need to be resolved; this does not discount the likelihood that a proposed therapy can be achieved. For example, there are many examples of proposed therapies using organic chemicals that are based solely on *in vitro* data, allowing one of ordinary skill in the art to have a reasonable degree of confidence that the therapy will be effective *in vivo*. In the present case, there is no rationale for concluding that the *in vivo* results obtained using animal models (*e.g.*, mice) would not reasonably correlate with human patients particularly in view of the fact that human bone marrow-derived cells form functional neural cells *in vivo*, as demonstrated by the Weimann *et al.* publication. The applicant respectfully submits that an application for patent is not required to show that a claimed method of treatment of a disease condition results in a cure of that disease condition, or even that clinical efficacy is achieved. The Federal Circuit has made it clear that the showing for therapeutic utility that is sufficient to satisfy the patent laws is not to be confused or equated with the showing required by the Food & Drug Administration for drugs, medical devices, and procedures. *Scott v. Finney*, 32 USPQ2d 1115 (Fed. Cir. 1994) and Manual of Patent Examining Procedure 2164.05. Given the state of the art, one of ordinary skill in the art can readily determine appropriate dosages, routes of administration, *etc.*, without resort to undue experimentation. Thus, the applicants respectfully submit that the subject specification enables the claimed cell-based transplantation methods.

The Office Action cites the Mezey *et al.* publication as evidence of difficulty in using hematopoietic stem cells to treat neurodegenerative disease. However, the Mezey *et al.* publication demonstrates that bone marrow-derived cells play a role in neurogenesis and that at least some of the neurons and glia present in the adult nervous system may be bone marrow-derived (see page 298, first column, of Mezey *et al.*). Page 301 of the Mezey *et al.* publication is cited in the Office Action as highlighting the difficulties with using bone marrow cells for therapy. Although the Mezey *et al.* publication states that growth factor treatment *in vitro* may be necessary to enrich or select for distinct cell types, this is not evidence of difficulty in using bone marrow cells for therapy, but is instead an indication that if specific differentiated cells are required, it is necessary to identify a growth factor that will provide the cells required. The methods of the subject invention involve the

use of stem cells, which are undifferentiated and differentiate upon administration into the brain. It is therefore unnecessary to obtain distinct cell types prior to administration.

The reference to the "temporal limits" in the Mezey *et al.* publication is of limited relevance. As taught at page 6, lines 3-15, of the specification, conventional neural cell transplantation techniques (*i.e.*, transplantation directly into the brain) can be used. Therefore, it is not necessary to use the circulation system as contemplated by Mezey *et al.* The route of administration utilized for the hematopoietic cells does not represent an obstacle to the practice of the subject invention. As indicated above, by this Amendment, the applicant has cancelled claims 7 and 14, which recited that the hematopoietic cells are genetically transformed to express a therapeutic heterologous gene product. Accordingly, the applicants respectfully submit that, given the teaching of the specification, one of ordinary skill in the art could carry out the claimed methods without the need for undue experimentation. In view of the foregoing remarks, reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

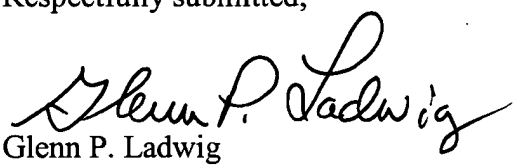
Claims 1-7 have been rejected under 35 U.S.C. §112, second paragraph, as indefinite. The applicants have amended the claims to correct the misspelling of "hematopoietic" where appropriate. Accordingly, reconsideration and withdrawal of the rejection under 35 U.SC. §112, second paragraph, is respectfully requested.

In view of the foregoing remarks and amendments to the claims, the applicant believes that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

The applicant invites the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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Attachments: Petition and Fee for Extension of Time
Associate Power of Attorney
Weimann *et al.* publication (*PNAS*, 2003, 100(4):2088-2093)